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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,590	10/17/2005	Yang Je Cho	69112(303198)	7799

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EXAMINER	
XIE, XIAOZHEN	
ART UNIT	**PAPER NUMBER**
1646	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,590	CHO ET AL.	
	Examiner	Art Unit	
	Xiaozhen Xie	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 May 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20050603*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *product sheet, seq. alignment*.

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The Information Disclosure Statement (IDS) filed 3 June 2005 has been entered. Applicant's amendments of the specification and the claims filed 9 May 2005 have been entered.

Claims 1-4 are pending and under examination.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: the signatures of the inventors are not dated.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Drawings

The drawings (in particular, Figures 1, 3a, 4, 5, 12 and 13) are objected to under 37 CFR 1.83(a) because they fail to show details as described in the specification. The fugures are not legible. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

The abstract of the disclosure is objected to for grammatical errors, e.g., "composition" should be "a composition"; "Bone Morphogenic Protein-7" should be set

forth at the first use of the acronym, "BMP-7"; and "sequence 1" should be "SEQ ID NO: 1". Further, it is unclear to exemplify new scar as "myofibroblast".

Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: *a composition for inhibiting a scar formation comprising an effective amount of a mature BMP-7 protein; wherein the effective amount of the BMP-7 is 50 ng/ml to 50 μg/ml or 0.1 ng/kg-1 μg/kg; and wherein the scar is a corneal scar,* does not reasonably provide enablement for a composition comprising a BMP-7 polypeptide of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: the breadth of the claims, the nature of the

invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See also *Ex parte* Forman, 230 USPQ 546 (BPAI 1986).

The claims are directed to a composition for inhibiting a scar formation, e.g., a corneal scar, comprising an effective amount of a BMP-7 polypeptide of SEQ ID NO: 1. The specification discloses that human amnion contains a component that can inhibit cornea scar formation. The specification discloses the extraction and identification of such a component. Applicant discloses that partial sequencing analysis reveals that the component/polypeptide shares sequence homology with BMP-7 (pp. 11, Table 2). Applicant further confirms that a BMP-7 polypeptide has scar formation inhibitory activity in cornea, by applying a commercial recombinant BMP-7 protein (R & D system) to rat cornea with alkali burn (pp. 12, and Figure 6). However, the commercial recombinant BMP-7 protein (R & D system) that Applicant tested which showed scar formation inhibitory activity in rat cornea is a fusion protein comprising human BMP-2 (hBMP-2 signal peptide and propeptide, amino acid residues 1-282 of hBMP-2) and human BMP-7 mature chain (amino acid residues 293-431 of hBMP-7). Upon the proteolytic removal of the signal peptide and propeptide (the hBMP-2 portion), it generates a mature recombinant BMP-7, which is a disulfide-linked homodimeric protein consisting of two 139 amino acid residue subunits (see product sheet). The amino acid sequence of SEQ ID NO: 1 shows a 95.5% homology to a fragment of BMP-7 signal peptide and

propeptide (human BMP-7 signal peptide spanning amino acid residues 1-29, propeptide spanning amino acid residues 30-292, and mature chain spanning amino acid residues 293-431). The instant SEQ ID NO: 1 shows homology to amino acid residues 1-139 of human BMP-7 precursor (see attached sequence alignment to human BMP-7 precursor and domains). Celeste et al. (Proc. Natl. Acad. Sci, 1990, 87:9843-9847) teach that BMP-7 is synthesized as a precursor molecule, and is processed by proteolytic cleavage to generate a mature form containing the C-terminal seven-cystein residue portion of the precursor. Fischer et al. (Mol. Cell.Neurosci., 2004, 27:531-542) teach that intraocular injection of a recombinant BMP-7 (mature BMP-7) exhibits a neuroprotective effect in the chicken retina. Applicant has not provided supporting evidence that a polypeptide homologous to a fragment of BMP-7 precursor comprising a signal peptide and a portion of the propeptide exhibits the scar formation inhibitory activity in rat cornea, nor does the prior art provide the compensatory guidance. Thus, the scope of patent protection sought by Applicant as defined by the claims fails to correlate reasonably with the scope of enabling disclosure set forth in the specification.

Due to the large quantity of experimentation necessary to determine if the claimed polypeptide which is homologous to a fragment of BMP-7 precursor, and comprises a signal peptide and a portion of the propeptide, can be used for inhibiting scar formation in cornea, the lack of direction/guidance presented in the specification, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes that BMP-7 activity is mediated through its mature form, which is, however, absent in the claimed SEQ ID NO: 1, the

unpredictability of the effects of protein structure on function, and the breadth of the claims, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie, Ph.D whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph.D. can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph. D.
December 29, 2007

Eileen B. O'Hara

EILEEN B. O'HARA
PRIMARY EXAMINER